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Kinetics and Mechanism of Oxidation of Leucine by Chloramine-T in Alkaline Media

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With 2 Figures

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Alkaline media oxidation of leucine by chloramine-T has been investigated. A first order dependence in chloramine-T and leucine and a near inverse first order dependence in hydroxide ion has been observed. Ionic strength had negligible effect while the effect of methanol addition was slightly negative. The oxidation process has been shown to proceed via two paths, one involving p-toluenesulfochloramide as the main oxidising species and the other involving hypochlorite ion, each interacting in a slow step with a leucine molecule leading to formation of monochloroleucine acid, which subsequently interacts with another molecule of p-toluenesulfochloramide or hypochlorite ion resp., yielding products.

The present paper incorporates the kinetics and mechanism of oxidation of leucine by chloramine-T in alkaline media. Being a potent oxidant in both acidic as well as in alkaline media ($E_{\text{red}} = 1.138$ V at pH 0.65), it has been used for the oxidation of several compounds[1–6] including amino acids[7]. However, the literature lacks with a detailed step by step mechanism of oxidation of leucine involving this oxidant.

Experimental

An E. Merck, pro analysi sample of chloramine-T was used and the solution stored in black coated bottles to prevent its photochemical deterioration[8]. Aqueous solution of leucine was obtained using A.R. B.D.H. sample. All other reagents viz. sodium perchlorate, potassium chloride and methanol were of analar grade. Triple distilled water was used throughout the course of the reaction and reaction stills blackened outside. A Leeds and Northrup pH meter was used for pH measurements.

Reactants were brought to thermostatic temperature (± 0.1°) and the reaction initiated by adding the appropriate amount of chloramine-T. The progress of the reaction was monitored by estimating unconsumed chloramine-T iodometrically.

Results

Reaction mixtures containing varying ratios of chloramine-T to leucine at pH 11.50 were allowed to equilibrate at 55° for 48 hours. From the results (Table 1), it is concluded that one mole of leucine consumes two moles of chloramine-T according to the stoichiometric equation (1) yielding nitrile, which was tested by conventional analytical method[9].

Table 1. *Stoichiometric Data, pH = 11.50, Temperature = 55 °C, Time = 48 hours, i = initial, f = final*

10^3 [Chloramine-T]$_i$ M	10^3 [Leucine] M	10^3 [Chloramine-T]$_f$ M	Stoichiometric ratio [Chloramine-T] : [Leucine]
0.5	0.0	0.5	—
1.0	0.5	0.0	2 : 1
1.5	0.5	0.5	2 : 1
2.0	0.5	1.0	2 : 1
2.5	0.5	1.5	2 : 1
3.0	0.5	2.0	2 : 1

$$\begin{aligned}&2\ CH_3C_6H_4SO_2NNaCl + (CH_3)_2CHCH_2CHNH_2COOH = \\ &= 2\ CH_3C_6H_4SO_2NH_2 + (CH_3)_2CHCH_2CN + CO_2 + 2\ NaCl\end{aligned} \tag{1}$$

Table 2. *Effect of Reactant's Concentration on the Reaction Rate.* pH = 11.50

10^3 [Chloramine-T] M	10^2 [Leucine] M	$k_1' \times 10^5$ sec^{-1} at 40°	45°
0.6	1.0	13.2	21.6
0.8	1.0	13.8	21.3
1.0	1.0	13.8	21.3
1.4	1.0	13.8	22.0
2.0	1.0	13.7	21.3
3.0	1.0	13.9	21.3
1.0	0.6	8.64	13.1
1.0	0.8	11.5	18.1
1.0	1.4	19.2	30.9
1.0	2.0	24.0	42.6
1.0	3.0	32.6	60.2

Oxidation of leucine was studied over a wide range of concentration of the reactants. The pseudo-first order rate constant (k_1') in chloramine-T was followed at all initial concentrations of the reactants (Fig. 1). A linear increase in first order rate constant was observed with increase

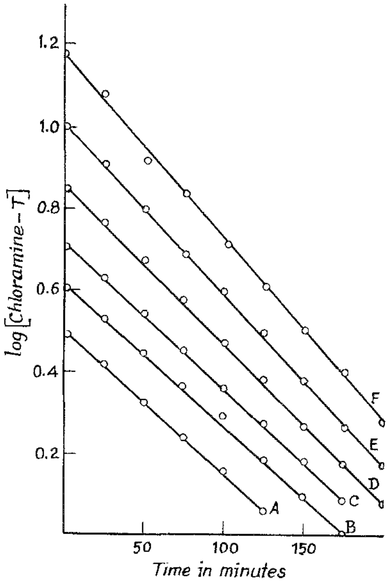

Fig. 1. First order rate plots at 40°, [Leucine] = 1.0×10^{-2} M, pH = 11.50, [Chloramine-T] = 0.6, 0.8, 1.0, 1.4, 2.0 and 3.0×10^{-3} M in A, B, C, D, E and F resp.

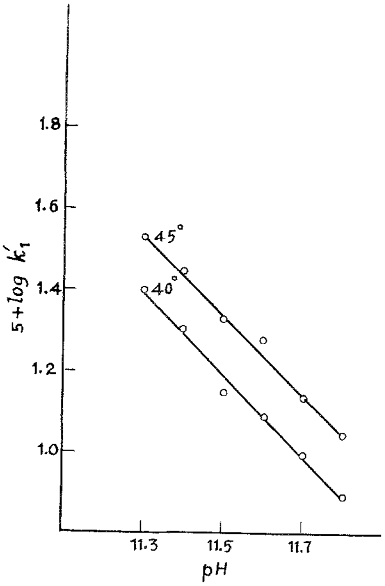

Fig. 2. Plots of log k_1' vs. pH, [Chloramine-T] = 1.0×10^{-3} M, [Leucine] = = 1.0×10^{-2} M, [$NaClO_4$] = 1.0×10^{-1} M

in leucine concentration and the second order rate constant calculated as $k_2' = k_1'/[\text{Leucine}]$ gave concordant values establishing a first order dependence in leucine also (Table 2).

Table 3. *Effect of Ionic Strength on the Reaction Rate.* [Chloramine-T] = $= 1.0 \times 10^{-3}$ *M*, [Leucine] $= 1.0 \times 10^{-2}$ *M*, pH = 11.50, Temp. = 40 °C

Salt concentration *M*	$k_1' \times 10^{-5}$ sec^{-1} for NaClO$_4$	KCl
0.00	13.8	13.8
0.20	13.5	14.1
0.28	13.4	13.6
0.40	13.1	14.1
0.48	13.5	13.9
0.60	13.5	13.8

Table 4. *Effect of Methanol on the Reaction Rate.* [Chloramine-T] = $= 1.0 \times 10^{-3}$ *M*, [Leucine] $= 1.0 \times 10^{-2}$ *M*, pH = 11.50, Temp. = 40 °C

[Methanol] %	$k_1' \times 10^{5}$ sec^{-1}
0	13.8
10	11.5
20	10.4
30	9.97
40	9.36
50	8.64

Table 5. *Effect of Temperature on Reaction Rate.* [Chloramine-T] = $= 1.0 \times 10^{-3}$ *M*, [Leucine] $= 1.0 \times 10^{-2}$ *M*, pH = 11.50

Temp., °C	$k_1' \times 10^5$ sec^{-1}	$k \times 10^5$ sec^{-1}	$A \times 10^{-5}$ sec^{-1}	$\Delta S^{\ne}$ e. u.	$\Delta H^{\ne}$ kcals/mole
35	9.59	3.03	2.23	— 35.3	13.4
40	13.8	4.35	2.23	— 35.3	13.4
45	21.3	6.74	2.43	— 35.1	13.4
50	34.5	10.9	2.79	— 34.8	13.4
55	48.0	15.2	2.72	— 34.9	13.3

A strong dependence of the rate to pH variation was observed. An increase in pH retarded the oxidation rate. A plot between log k_1' and pH (Fig. 2) gave straight lines with slopes — 0.98 and — 0.97 at 40 °C and 45 °C resp., establishing a near inverse first order dependence of the rate in hydroxide ion concentration.

Ionic strength variation had negligible effect (Table 3), while the effect of methanol addition was slightly negative (Table 4).

Average values of the rate parameters viz. energy of activation, frequency factor (A), entropy of activation ($\Delta S^{\neq}$) and heat of activation ($\Delta H^{\neq}$) have been computed as 14.0 kcals/mole, $2.48 \times 10^5\ \mathrm{sec}^{-1}$, -35.1 e.u. and 13.4 kcals/mole resp. from the rate study measurements carried out at five temperatures (Table 5).

Discussion

An aqueous solution of chloramine-T hydrolyses as follows[10]:

$$CH_3C_6H_4SO_2NNaCl + H_2O \rightleftharpoons CH_3C_6H_4SO_2NHCl + NaOH \qquad (2)$$

$$CH_3C_6H_4SO_2NHCl + NaOH \rightleftharpoons CH_3C_6H_4SO_2NH_2 + Na^+ + ClO^- \qquad (3)$$

$$2\, CH_3C_6H_4SO_2NHCl \rightleftharpoons CH_3C_6H_4SO_2NCl_2 + CH_3C_6H_4SO_2NH_2 \qquad (4)$$

$$CH_3C_6H_4SO_2NCl_2 + NaOH \rightleftharpoons CH_3C_6H_4SO_2NHCl + Na^+ + ClO^- \qquad (5)$$

The oxidising species of chloramine-T are chloramine-T itself, p-toluenesulfochloramide, hypochlorite ion and dichloramine-T, any one among these being the main oxidising species. In an alkaline media, dichloramine-T does not exist (eq. 5). As an increase in hydroxide ion concentration (or pH) decreases the reaction rate, p-toluenesulfochloramide is certainly the main active oxidising species in this case.

The proposed mechanism involves leucine molecule reacting in a slow step with p-toluenesulfochloramide to form intermediate monochloroleucine acid and which in a subsequent fast step interacts with another molecule of p-toluenesulfochloramide yielding products. The essential steps thus involved are:

$$CH_3C_6H_4SO_2NNaCl + H_2O \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} CH_3C_6H_4SO_2NHCl + NaOH \qquad (2)$$

$$\begin{gathered} CH_3C_6H_4SO_2NHCl + (CH_3)_2CHCH_2CHNH_2COOH \xrightarrow[\text{slow}]{k_2} \\ CH_3C_6H_4SO_2NH_2 + (CH_3)_2CHCH_2CH(NHCl)COOH \end{gathered} \qquad (6)$$

$$\begin{gathered} (CH_3)_2CHCH_2CH(NHCl)COOH + CH_3C_6H_4SO_2NHCl \xrightarrow[\text{fast}]{k_3} \\ CH_3C_6H_4SO_2NH_2 + (CH_3)_2CHCH_2CN + CO_2 + 2\, HCl \end{gathered} \qquad (7)$$

Application of steady state treatment, followed by reasonable approximation $k_{-1}\,[NaOH] \gg 2\, k_2\, [(CH_3)_2CHCH_2CHNH_2COOH]$, yields the rate law as

$$-\frac{d}{dt}[\text{chloramine-T}] = \frac{2\, k_1 k_2\, [\text{Chloramine-T}][(CH_3)_2CHCH_2CHNH_2COOH]}{k_{-1}\, [NaOH]} \qquad (8)$$

in accordance with the experimental observations.

To account for the deviation of order in hydroxide ion concentration from — 1, it is proposed that an insignificantly small fraction of the overall reaction proceeds via another path involving hypochlorite ion in steps (6) and (7), leading to the rate law as

$$-\frac{d}{dt}[\text{Chloramine-T}] = k''[\text{Chloramine-T}][(CH_3)_2CHCH_2CHNH_2COOH] \quad (9)$$

where k'' is a constant.

Rate law (8) predicting an inverse first order dependence in hydroxide ion concentration and rate law (9) predicting a zero order dependence in hydroxide ion concentration satisfactorily accounts for the observed deviation of order in hydroxide ion concentration.

A slight negative methanol effect successfully accords with this alternative path. Negligible influence of ionic strength variation is also in agreement with the rate determining slow step in both the processes.

Thus it has been possible to interpret the results of oxidation of leucine by chloramine-T in alkaline media as a two process reaction, the predominating path involving p-toluenesulfochloramide as the oxidising species and the insignificantly small path involving hypochlorite ion as the oxidising species.

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